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Swiss Appendix to the International Trial Protocol

"Tranexamic acid for hyperacute spontaneous IntraCerebral Haemorrhage (TICH-3)"

(TICH-3; International Version 4.2 30/03/2023)

In the following, we describe amendments for the conductance of the trial entitled "Tranexamic acid for hyperacute spontaneous IntraCerebral Haemorrhage – TICH-3" in Switzerland:

1. **Pregnancy**: All female patients in childbearing age (<49 years) undergo pregnancy testing before participation in this study. Pregnancy testing will be done either by urine or blood test.

2. **Recruitment**: All participants must give informed written consent. If patients are unable to give informed written consent themselves as defined in article 24 "Humanforschungsgesetz", next-to-kin/legal representative must give informed written consent. If patients are unable to give informed written consent themselves, and if consent cannot be obtained by next-to-kin/legal representative within inclusion window recruitment will be done by an independent physician according to article 30 "Humanforschungsgesetz". Patient information and consent form have to be in official Swiss language.

3. **Day 180 follow-up**: Follow-up for D180 will exclusively occur through telephone interviews. Patients will be contacted by a study nurse or clinical trial coordinator from the site where they were enrolled and treated.

Revocation of consent and refusal of Subsequent Consent:

As ICH is an emergency and the intervention studied in this trial has to occur within a narrow time window, patients might be enrolled by different modalities, depending on their capacity to consent. The different enrollment scenarios, potential revocation or refusal of consent, and the respective consequences on further utilization of collected data are briefly described below. The described scenarios are in accordance with the Swiss Federal Act on Research involving Human Beings (Human Research Act, HRA Art. 15-17 and Art. 31).

Patient with <u>capacity</u> to consent with revocation of consent

4. **Consent and enrollment by the patient:** A patient who initially gave consent can recall consent at any time during the study. This is considered a revocation. In such a case, all study activities will be immediately terminated, and data collected up until this point will be utilized for the final analysis in an encrypted format.

Patient with (temporary) <u>incapacity</u> to consent

5. **Consent and enrollment by a legal representative (LAR) or a relative (next-of-kin):** In cases where the LAR/next-of-kin provides proxy consent, any subsequent refusal by the patient is considered a revocation, as the proxy consent was initially granted. In such a case, all study activities will be immediately terminated, and data collected up until this point will be utilized for the final analysis in an encrypted format.

6. **Enrollment by an independent physician:** Enrollment by an independent physician does not equate patient or LAR/next-of-kin consent. LAR/next-of-kin consent must be sought as soon as possible after the enrollment of a patient by an independent physician. Should the LAR/next-of-kin or the patient decline consent thereafter, it constitutes a subsequent refusal. In such a case, all study activities will be immediately terminated. Personal data collected up until this point will be deleted. Safety data will be utilized for the final analysis in a fully anonymized format so as not to impair the validity and integrity of the study results.

7. **Follow-up of study participants after adverse events related to the trial:** Patients will be closely monitored for adverse events during the hospitalization period. Details

of pre-specified safety outcomes are given in the protocol. The IMP is given once for 8 hours, and has a very short half-life, hence the likelihood of adverse events occurring after discharge is low. Prior to hospital discharge, patients or their next-of-kin/legal representative will be reminded to promptly report any adverse events. Adverse events related to the trial will also be inquired about during the Day 180 Follow-up interview. The investigator ensures that subjects receive appropriate medical care in the event of adverse events, related to the trial.

8. We confirm that the participants initials will NOT be used in the participants data collection in the electronic case report form or in generating the participant number.

Nottingham, 28.03.2024

DR. NIKOLA SPRIGG.

Electronic signature

Professor Nikola Sprigg
Chief Investigator TICH-3
On behalf of the Sponsor